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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER	
BASHAM,D	
ART UNIT	**PAPER NUMBER**
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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

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File copy

Office Action Summary	Application No. 08/466,343	Applicant(s) Li, et al.
	Examiner Daryl A. Basham	Group Art Unit 1646

☒ Responsive to communication(s) filed on *June 12, 1997 and July 11, 1997*.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *21-54* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *21-54* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. The amendments filed June 12, 1997 and July 11, 1997 have been entered. The Advisory Action mailed on July 11, 1997 has been vacated as the Office Action mailed February 10, 1997 was not a Final Rejection. The Office acknowledges that the prior Office Action of February 10, 1997 should not have been sent under 1.116 as a Final Rejection and that the Advisory Action of July 11, 1997 was sent in error. An action on the merits is provided below.

2. Claims 21, 22, 25, 28, 30-32, 34-36, 38 and 40 are objected to because of the following informalities: In claim 21, the unattached phrase "a polypeptide comprising amino acid 2 to 352 of SEQ ID NO: 2" is extraneous material. In claims 21, 22, 25, 28, 30-32, 34-36, 38 and 40 where the description or claims of a patent application discuss a sequence listing that is set forth in the "Sequence Listing" in accordance with paragraph (C) of MPEP § 2422, reference must be made to the sequence by use of the assigned identifier, in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application. Appropriate correction is required.

Response to Amendment

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 21, 22, 25, 28, 30-32, 34-36, 38, 39, 45-50, 52 and 53 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for polynucleotides encoding an amino acid sequence as set forth in SEQ ID NO: 2, does not reasonably provide enablement for polynucleotides encoding a "mature" polypeptide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicants argue that "mature" is delimited by minor differences in sequence as set forth in SEQ ID NO: 2 (e.g., the presence or absence of N-terminal methionine or the addition of sequences which allow for purification), however, the specification does not limit "polypeptides encoding the mature polypeptide" to these modifications and includes, for example, "the coding sequence for the mature polypeptide and additional coding sequence such as a transmembrane or intracellular domain" (at page 7, lines 21-23). Since the instant polypeptide has been putatively assigned receptor properties (i.e., comprises at least a integral membrane domain), and as there is no disclosure for replacement of domains in the specification, then polynucleotides encoding "mature" polypeptides also include gene products with multiple integral/transmembrane domains. Such molecules are not within the alleged definitions recited in Applicant's argument (i.e., beyond the scope of the presence or absence of methionine or fused marker in facilitating isolation). Therefore, no distinction is made using the modifier "mature" which makes apparent the structure, function or sequence peculiar to the instant polypeptide so designated.

Claims 21, 22, 25, 28, 30-32, 34-36, 38 and 40 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for polynucleotides encoding an amino acid sequence as set forth in SEQ ID NO: 2, does not reasonably provide enablement for all of the polynucleotides that are 95% identical to a polynucleotide encoding a structurally undefined polypeptide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicants argues that the specification specifically defines HDGNR10, enumerating various properties which allegedly distinguish and make apparent the abbreviation, structurally as claimed. However, none of the recited properties are listed in the claims. Therefore, as the abbreviation does not inherently represent any particular nucleic acid sequence, the limitation that a polynucleotide be 95% identical is meaningless in the absence of an appropriated reference molecule (e.g., SEQ ID NO: 1 and/or 2). For these reasons, the rejection of record is maintained.

Claims 21, 22, 25, 28, 30, 31, 34, 35, 38, and 40 are rejected under 35 U.S.C. 102(b) as being anticipated by Chuntharapai et al.

Applicants argue that the Office "did not appreciate the cross-references of such terms with the sequence listing, figures and deposited clone in the specification" as they relate to the terms "mature HDGNR10 protein" or " mature HDGNR10 polypeptide". Again, Applicants suggest that the cross-referenced material be read into the claims since none of the enumerated properties associated with said references are recited as claim limitations. Therefore, because the

instant specification uses "HDGNR10" and "G-protein chemokine receptor" interchangeably and as the instant claims depend solely on the abbreviation as a [structural] reference to define the polynucleotide, the claims embrace all G-protein chemokine receptors. For these reasons, the rejection of record is maintained.

Claim Rejections - 35 U.S.C. § 112

4. Claims 38-41 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for producing a polypeptide comprising amino acids as set forth in SEQ ID NO: 2, does not reasonably provide enablement for producing all polypeptides having a sequence other than SEQ ID NO: 2 which have similar functional properties to the polypeptide as set forth in SEQ ID NO: 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

By claiming polynucleotide sequences using a polypeptide as the reference molecule (e.g., claim 21, from which claims 38-41 depend), all degenerate polynucleotides capable of encoding the amino acid sequence as set forth in SEQ ID NO: 2 are embraced. If , for example, all of the third positions of the codons are replaceable by wobble hypothesis rules (given nucleic acids of equal length) to give the same amino acid sequence by degeneracy of the genetic code, a nucleic acid approaching 66.6% identity to the naturally occurring sequence would be expected to be present in the population of molecules. However, a polynucleotide which is 95% identical to said

perfectly degenerate polynucleotide (e.g., the overall homology could be as low as 64%) could not be used, predictably, to produce the polypeptide as set forth in the instant SEQ ID NO: 2 by recombinant means having the required functional properties since the identity of the instant polypeptide is based solely on structural relatedness to similar G-proteins (i.e., has not been assayed for function), wherein it cannot be known *apriori* what sequences should be changed such that ligand binding fidelity is maintained (e.g., there is no disclosure which delimits the requisite amino acids that allow for ligand binding nor is the cognate ligand disclosed). As such, the limitations of the claims embrace polynucleotides which encode polypeptides that are not envisaged by the specification. Therefore, as the specifications fails to adequately provide guidance or examples of a polynucleotide having 64% identity with the naturally occurring polynucleotide as set forth in SEQ ID NO: 1, one skilled in the art could not make or use the embraced polynucleotides without undue experimentation because the changes in polypeptide sequence encoded by such a polynucleotide would be chosen arbitrarily.

5. Claims 21-54 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 21-54 recite "...% identity". This phrase has unambiguous meaning when it is applied to the comparison of two sequences of equal length, however, sequences of unequal length are evidently considered to be comparable by this standard. It is not clear as to how gaps are to be assessed in determining identity where gaps are required to optimally align two

sequences of unequal length. This ambiguity may be demonstrated by the following examples: consider two sequences, ABCDEF and ABEF. These could be compared in four ways:

ABCDEF	4/6 = 67%	ABCDEF	2/6 = 33%
AB---- EF	4/4 = 100%	ABEF	2/4 = 50%

In the absence of a disclosure of the algorithm by which "...% identity" is to be determined, the claims can only be considered definite if comparisons are limited to sequences of identical length. To illustrate this issue, the Examiner has cited George, et al. (1988) which teaches that "the results of the analysis are entirely dependent on the choice of scoring rules" (page 130, column 2, lines 4-6). It is apparent that an algorithm is required to determine the "% homology".

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daryl A. Basham, Ph.D., whose telephone number is (703) 305-2150. The examiner can normally be reached Monday through Friday from 9:00 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Stephen Walsh, can be reached on (703) 308-2957.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Stephen Walsh

STEPHEN WALSH
SUPERVISORY PATENT EXAMINER
GROUP 1800

dab
March 26, 1998